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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,792	06/22/2001	Tobias Meyer	0459-0570P	9673

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EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/787,792	Applicant(s) MEYER, TOBIAS	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *18 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *8-10,12 and 26-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-7,11,13-25 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-6 in Paper No. 11 are acknowledged. The traversal is on the ground(s) that Group I, claims 1-6 and Group II, claims 8-25 have improperly applied the unity of invention guidelines. Therefore, these two groups should be rejoined. Upon careful reconsideration of the restriction requirement and request to rejoin Groups I and II, the restriction and request are partly granted. However, claims 8-10, which contain the limitation, library, will not be examined with the rejoined Groups. A prior art reference without the library will not render obvious the claim to a library. Applicant's election of the species: mammalian cell; plasma membrane and kinase are noted. As stated in the last Office action, because of structural differences in e.g., proteins, restriction between the species is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-10, 12 and 26-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Specification

The disclosure is objected to because of the following informalities:

1. The specification recites for a drawing, Fig. 1 E. However, there is no Fig. 1E.

2. Spelling errors too numerous to mention specifically. **Examples** of these errors are: "hydrophilic" at page 8,line 19; "stable" at page 10, line 1; "membreane" at page 10, line 12.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

The listing of references in the specification, pages 29-31, is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into

the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

Claims 1-7, 11, 13-22, 24-25 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for GFP as the detectable group and isoforms of CaMKII α and β, does not reasonably provide enablement for a first and second heterologous protein conjugates, fragments of the protein and any type of cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The enabling disclosure provided in the specification is not commensurate in scope with the broad claimed invention. The broad claimed invention recites for any proteins that interact with each other in a cell. However, because of the structural differences of proteins, primary sequence or conformation, it would it take undue experimentation to determine which proteins, singly, or in combination would interact in the presence of a cell. All of the examples, provided in the specification relates to single embodiments for each of the numerous variables of the claims. The

Examples in the specification, which have been provided as a guide to direct a skilled artisan, clearly demonstrates that even for these specific binding kinase isoforms, applicant cannot predict the presence or absence of the two proteins in different regions of a single cell. There is no indication in the specification that the species demonstrated therein can be applied a priori to any type of proteins contained in any type of cell. To practice the claimed invention, an undue amount of experimentation would be required. The factors to be considered in a determination of undue experimentation are disclosed in *re Wands*, (U.S.P.Q. 2d 1400 (CAFC 1988). These factors are as follows: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of the claims.

1). The specification fails to give adequate direction and guidance in how to readily go about determining which protein binding pair can be contained in all cell to detect binding of one pair to the cell and not to the other.

2). The specification failed to provide working examples for any other protein-protein binding pair or detectable groups

that can be attached to either one or both of the proteins, the cell that can contain each protein, the assurance that it is the specific protein that binds to a cell or influenced a cell binding and not the other protein of a conjugate. As stated above, the single working example in the specification provides only specific cells as influenced by the kinase isoforms i.e., its localization and determination of whether one proteins binds or not.

3). The breadth of the claims encompasses a large diversity of not only proteins but its fragments, its binding effect, the means of detection and other broadly undefined variables. It is well known in the art that it is often difficult to know what the expression level of specific peptides or peptide fusions is; in many cases, even an average measure of expression level is difficult to obtain. The diversity of the inserts is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert.

4). The state of the prior art is such that while techniques or the expression of determinants on the cell surface exist only for the well studied cells and proteins influencing said cell, however, even with the specific cell type and

proteins, applicants have shown in their specification that limitations exist.

5). The art is inherently unpredictable because even one protein binding pair is detected, it is not possible to predict what effect the binding pair has for a different cells or a cell with a different binding pair. Likewise, it is not possible to predict which fragments or variations of amino acids or combinations of amino acids would result in the proper binding of the protein and therefore proper contact with the cell. It is generally known that the conformational freedom that promotes binding, e.g., by modifying the peptides into the protein sequences, might be restricted which may likely perturb the function and stability of the fusion in ways difficult to predict and measure. Some proteins accommodate insertions (variations) at numerous sites throughout their primary sequence. Others are much less accommodating. It is difficult in general to predict which proteins are robust to insertions, and which sites in a particular protein are best suited to insertion of multiple independent sequences.

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined variables would display a protein binding domain having the desired activity without undue experimentation. Applicants do not adequately enable persons

skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 11, 13-25 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps intermediate between steps (a) and (b). It is not clear from the limited process steps how simply providing a cell with the protein components result in the positive or negative detection of the protein interactions i.e., the first protein of interest binding only to the second protein of interest. As the succeeding statement recites' "binding of said detectable group to said

internal structure" makes it confusing. The terms "first" and "second" are relative terms. It is not clear from the claimed context the differentiating characteristics or features of these claims. "Protein of interest" is ambiguous as to the basis by which of said protein selection.

B). Claims 3 and 4 recite a nucleic acid that encodes the fusion protein which broadens the base claim. The base claim does not recite for a nucleic acid. Is it nucleic acid or protein intended? "Said fusion protein" lacks antecedent basis of support from the base claim. Also, it is not clear as to the difference between the fusion and conjugate proteins, within the claimed context.

C). The metes and bounds of the claimed "members of a specific binding pair" in claim 6 is ambiguous i.e., as to the members contain in each protein and how each is determined to be a specific binding pair.

D). Claim 7 broadens the base claim 1. The base claim does not recite for a test compound to test for the binding effect or lack thereof. This is confusing since the base claim recites a detectable group that detects said binding.

E). Claims 24 and 25 are unclear as in what aspects the two proteins are the "same" or "different".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 11, 15-22, 24-25 and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Shirai et al (Japanese Journal of Pharmacology, 1998).

The claimed method of detecting the interactions between heterologous proteins in a cell wherein one of the heterologous conjugate comprises a detectable label as GFP is fully met by the process of Shirai. See the entire abstract. Shirai discloses a conjugate of delta, gamma and epsilon PKC fused with GFP. All fusion proteins are expressed in the CHO-K1 cells wherein each fusion proteins showed a specific subcellular localization. The specific method of Shirai employing specific components fully meets the broad claimed method.

Claims 1-7, 11-14, 15-22, 24-25 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Knippschild et al (Oncogene, 1997).

The claimed method of detecting the interactions between heterologous proteins in a cell wherein one of the heterologous conjugate comprise a detectable label as GFP is fully met by the process of Knippschild et al. See the entire abstract. Knippschild discloses a conjugate of gamma and epsilon kinase fused with GFP. All fusion proteins are expressed in the murine cells. See the entire abstract. The specific method of Knippschild employing specific components fully meets the broad claimed method.

Claim 23 is free of prior art.

REASSIGNMENT OF LOCATION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit **1639**.Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
November 18, 2002